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The Worst Headache of Life: Evaluation of Nontraumatic Subarachnoid Hemorrhage

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While the "worst headache of life" has a differential diagnosis, acute subarachnoid hemorrhage must be the primary diagnostic consideration. Approximately 1%-4% of patients presenting to the emergency department with severe headache have subarachnoid hemorrhage (1). Subarachnoid hemorrhage is the number one secondary cause of incapacitating abrupt onset headache, while migraine headache is the number one primary cause (2). There are approximately 30,000 cases of nontraumatic subarachnoid hemorrhage in the United States each year (2, 3).

The classic presentation of nontraumatic subarachnoid hemorrhage is an acute onset, severe headache which reaches its maximum intensity within minutes, often referred to as the "thunder clap" headache (2). The headache is usual bilateral in nature and more often occipital than frontal. There may be associated neck stiffness, photophobia, nausea, vomiting and possibly obtundation or coma. Physical examination may show retinal hemorrhages, nuchal rigidity, or focal neurological signs. An altered level of consciousness is seen in approximately one third of patients while meningeal irritation signs are seen in up to 85% of patients and virtually all have nausea (4). Retrospectively, a sentinel headache caused by a small subarachnoid hemorrhage or warning leak has been reported in 15% to 59% of patients before a major rupture of a saccular aneurysm (5). Sentinel headaches usually persist for hours to days.

The differential diagnosis of a thunder clap headache includes aneurysm thrombosis without rupture, "leakage" into an aneurysm wall, aneurysm rupture with subarachnoid hemorrhage, cerebral vein/dural venous sinus thrombosis, localized meningeal inflammation, nonaneurysmal perimesencephalic hemorrhage, first or worst migraine headache attack, benign exertional headache, and benign thunderclap headache [no associated subarachnoid hemorrhage] (2). Since early recognition and surgery may benefit patients with aneurysm rupture, all patients with thunderclap headache require evaluation for subarachnoid hemorrhage. In North America, 75% to 90% of nontraumatic subarachnoid hemorrhage is caused by aneurysm rupture (6). Other sources of nontraumatic subarachnoid hemorrhage include nonaneurysmal perimesencephalic hemorrhage, arteriovenous malformations (AVM), including the rare spinal AVM, intracranial arterial dissection, primary or metastatic brain tumors which hemorrhage, hypertensive parenchymal hemorrhage with subarachnoid extension, anticoagulant therapy, and vasculopathy.

The Hunt and Hess Scale for clinical grading of subarachnoid hemorrhage, Table 1 (7), is a useful tool for communication during referral conversations. There is also a correlation with the patient's grade and likelihood of a favorable outcome from early intervention. Grades are I, II, and III have a favorable prognosis.

The primary diagnostic modalities in the evaluation of subarachnoid hemorrhage include noncontrast computed tomography (CT) scan and, if negative, a lumbar puncture with cerebrospinal fluid (CSF) spectrophotometry. The probability of detecting subarachnoid hemorrhage of CT scans performed at various intervals after the ictus is: day 0, 95%; day 3, 74%; day 7, 50%; day 14, 30%; and day 21, almost zero (8, 9, 10). The probability of detecting xanthochromia with spectrophotometry in the CSF at various times after a subarachnoid hemorrhage is: 12 hours, 100%; 7 days, 100%; 14 days, 100%; 21 days, more than 70%; and four weeks, more than 40% (8). It is important to note that the sensitivity of CT in detecting subarachnoid hemorrhage decreases with time, and may miss up to 5% of cases even in the first 12 hours after symptom onset. A lumbar puncture

must be performed if the CT scan is negative. An opening pressure should also be performed, as an elevated opening pressure may suggest a cerebral vein/dural venous sinus thrombosis (2). Magnetic resonance (MR) imaging is not as sensitive in the detection of acute subarachnoid hemorrhage and does not play a role in the initial diagnostic evaluation. CT has greater availability, lower expense, and faster scanning times.

Acute subarachnoid hemorrhage appears as high attenuation on noncontrast CT within the subarachnoid spaces (Figure 1). Blood will insinuate within the sulci over the cerebral convexities as it mixes with CSF (Figure 2). A focal cisternal or parenchymal hemorrhage may suggest the location of a ruptured aneurysm. Focal anterior interhemispheric blood is usually due to an anterior communicating artery aneurysm rupture. Blood in the sylvian fissure may be due to a middle cerebral artery, internal carotid artery terminus, or posterior communicating artery aneurysm rupture (11). Posterior communicating artery aneurysms may be associated with third cranial nerve palsies and often bleed into the temporal lobe. Posterior inferior cerebellar artery aneurysms often bleed into the fourth ventricle. Nonthrombosed aneurysms may be seen as a well delineated, isodense to slightly hyperdense mass located somewhat eccentrically in the suprasellar cistern or sylvian fissure. After detection of hemorrhage by CT or LP, the next step in the evaluation is referral to neuroradiology for a four vessel cerebral angiogram.

While CT and MR angiography have a high sensitivity and specificity in intracranial aneurysm detection, the gold standard for evaluation of acute subarachnoid hemorrhage is conventional catheter angiography. Approximately 90% of all intracranial aneurysms arise from the anterior cerebral circulation while 10% arise from the posterior circulation. The most common locations are the anterior communicating artery (35%), posterior communicating artery origin (30%), middle cerebral artery bi- or trifurcation (25%), basilar artery tip (5%), and the posterior inferior cerebellar artery and other sites distal to the circle of Willis (5%) (12). Up to 30% of patients with aneurysmal subarachnoid hemorrhage have multiple intracranial aneurysms (13). Patent aneurysms are seen as a contrast filled outpouching from the vessel wall on angiography (Figure 3 a, b). Ruptured aneurysms typically have an irregular or lobulated appearance (Figure 3c). Localized vasospasm and subarachnoid hemorrhage are also helpful signs of aneurysm rupture, particularly in those patients with multiple aneurysms.

Risk factors for development of intracranial aneurysms include autosomal dominant polycystic kidney disease, hypertension, aortic coarctation, alpha-1-antitrypsin deficiency, connective tissue diseases such as Ehlers-Danlos syndrome, fibromuscular dysplasia, and a family history of berry aneurysms. Other etiologies include drug abuse (cocaine), infection (mycotic aneurysms), neoplasm, or trauma.

In approximately15-30% of patients with nontraumatic subarachnoid hemorrhage, no aneurysm is found despite a complete four vessel cerebral angiogram (14, 15). These patients fall into two distinct subsets: a nonaneurysmal perimesencephalic hemorrhage pattern and an "aneurysmal" pattern, at risk for rebleeding, cerebral ischemia, and neurological deficit. In the first subset, the hemorrhage is typically anterior to the brainstem and within the interpeduncular fossa or ambient cisterns and is thought to result from rupture of small pontine or perimesencephalic veins (16). In the second subset of patients, subarachnoid hemorrhage fills the suprasellar cistern and extends into the

sylvian or anterior interhemispheric fissures. Repeat four-vessel cerebral angiography demonstrates an aneurysm in 5% to 10% of these cases (16, 17). Non-identification of the aneurysm on the first angiogram may be secondary to local vasospasm with incomplete filling of the aneurysm.

Acute subarachnoid hemorrhage carries a mortality rate of 25% in the first 24 hours and 50% within three months (18, 19). Causes of sudden death include a large intraparenchymal hematoma, destruction of brain tissue, acute hydrocephalus, increased intracranial pressure, myocardial ischemia, cardiac arrhythmias, and respiratory failure (19). Of the patients that reach a major medical center the leading causes of death are the sequelae of the initial hemorrhage, recurrent aneurysmal rupture and vasospasm with ischemic stroke. While the potential complications of subarachnoid hemorrhage are extensive, the primary goal of medical management is to address the leading causes of death by trying to prevent vasospasm and recurrent hemorrhage.

Prevention of vasospasm is predominantly via administration of a calcium channel blocker such as nimodipine, which decreases blood pressure but increases cerebral blood flow (19). Maintaining adequate hydration is also important. Vasospasm typically occurs seven days (5-10 days) after the subarachnoid hemorrhage. Transcranial Doppler evaluation is helpful in monitoring the development of vasospasm by detecting elevated intracranial arterial velocities. Once vasospasm occurs, medical therapy is aimed at increasing cerebral blood flow, predominantly with volume expansion and drug-induced hypertension. Vasospasm is seen most frequently in the distal internal carotid artery and the proximal portions of the anterior and middle cerebral arteries, regardless of the location of the aneurysm rupture (19). Transluminal angioplasty is extremely successful in dilating vasospastic arteries (20).

The prevention of recurrent hemorrhage, which is highest immediately after the initial subarachnoid hemorrhage, is through early surgical or endovascular treatment of the ruptured aneurysm. Endovascular therapy with platinum coils was introduced in 1990 as an alternative to surgical clipping (21). The International Subarachnoid Aneurysm Trial (ISAT) demonstrated a significant risk reduction with endovascular therapy over surgery for ruptured aneurysms amenable to either therapy (22). Endovascular treatment is particularly useful in posterior circulation aneurysms, such as a basilar tip aneurysm, in which the surgical approach is extremely difficult. A large aneurysm neck-to-dome ratio is the biggest exclusion factor for endovascular therapy. Currently, a multi-center trial investigating endovascular stents which can be placed over wide neck aneurysms allowing safe deployment of coils through the stent is underway. With the exception of difficult access to posterior circulation aneurysms, surgical clipping is an effective and definitive treatment modality of ruptured aneurysms. Patients with subarachnoid hemorrhage should be evaluated in treatment centers that offer both neurosurgery and neuroendovascular treatment, allowing the neurosurgeons and interventional neuroradiologists to assess the advantages and disadvantages of clipping or coiling for each individual patient.

In summary, nontraumatic subarachnoid hemorrhage is the most common secondary cause of the worst headache of life and 75% to 90% of nontraumatic subarachnoid hemorrhage is caused by aneurysm rupture. Since early diagnosis and treatment of aneurysm rupture may improve the patient's outcome, all patients presenting with the worst headache of life require evaluation for subarachnoid hemorrhage with a

noncontrast CT scan and a lumbar puncture if the CT scan is negative. Once subarachnoid hemorrhage is detected, a catheter angiogram should be performed, preferably at a facility with both interventional neuroradiologists and neurosurgeons. This allows the patient to undergo aneurysm coiling or clipping and be appropriately managed for common complications such as vasospasm or hydrocephalus.

Table 1. Hunt and Hess Scale for Clinical Grading of Subarachnoid Hemorrhage

Grade I: Asymptomatic, minimal headache, or slight nuchal rigidity

Grade II: Moderate to severe headache, nuchal rigidity, neurologic deficit confined to cranial nerve palsy

Grade III: Drowsiness, confusion, or mild focal deficit

Grade IV: Stupor, moderate to severe hemiparesis, possibly early decerebrate rigidity, and vegetative disturbances

Grade V: Deep coma, decerebrate rigidity, moribund appearance

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FIGURE LEGEND

Figure 1. Noncontrast CT scan demonstrating dense subarachnoid hemorrhage in the suprasellar and basilar cisterns as well as within the fourth ventricle. Note that the temporal horns of the lateral ventricles are dilated, consistent with hydrocephalus.

Figure 2. Noncontrast CT scan demonstrating subarachnoid hemorrhage layering within the sulci in the bilateral frontal regions. The location of this hemorrhage is suggestive of an anterior communicating artery aneurysm rupture.

Figure 3a. Right common carotid artery injection digital subtraction angiography anteroposterior view demonstrating an anterior communicating artery aneurysm. 3b. 3-dimensional reconstruction from a rotational angiogram on the same patient clearly demonstrating the anterior communicating artery aneurysm. 3c. Right common carotid artery injection digital subtraction angiography lateral view demonstrating a posterior communicating artery aneurysm in a different patient with classic lobulated margins, consistent with rupture.